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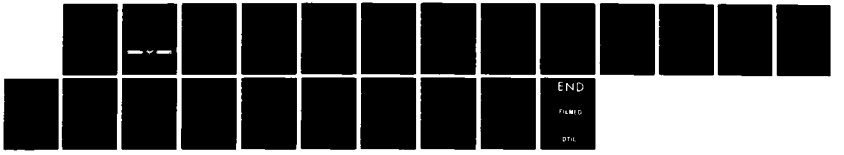

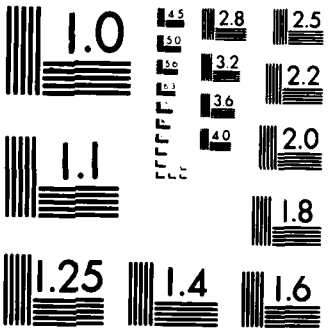

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REPORT NO. T1/85

EFFECTS OF ATROPINE DOSAGE LEVELS ON MILITARY MAP PLOTTING

US ARMY RESEARCH INSTITUTE OF ENVIRONMENTAL MEDICINE
Natick, Massachusetts

January 1985

UNITED STATES ARMY
MEDICAL RESEARCH & DEVELOPMENT COMMAND

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A study was conducted to determine the effects of several atropine dosage levels (0, 0.5, 1.0, 2.0, 3.0, 4.0 mg, administered intramuscularly) combined with ambient heat exposure (40°C, 40% RH) on the ability of soldiers to perform a task consisting of plotting sector-grid coordinate locations on military maps. Following acclimatization, eight soldier volunteers plotted grid coordinates on military sector maps for a ten-minute period daily as part of a larger study, under different series of daily drug administrations combined with heat exposure. No differences were observed in performance of

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the task between drug test days and control days, either in number of targets plotted or in mean errors. Furthermore, any drug effects on performance were so slight as to be offset by noticeable improvement in performance of the task due to practice. These results would seem to support the feasibility of atropine utilization as a chemical defense antidote for combat operations, since it had no observable effect on performance of an important and widely-employed operational military task.

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2. Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

Effects of Atropine Dosage Levels on Military Map Plotting

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FOREWORD

This study was conducted as part of an inter-Division project sponsored by the US Army Research Institute of Environmental Medicine to assess the effects of injected atropine on the military performance of acclimatized troops operating under hot-humid conditions. The dosage levels employed were those judged to be relevant on the basis of antidote dosage levels adopted by the US Army as standard for combat operations. Although a variety of physiological and psychological measures were utilized, only those obtained by the author are reported here.

TABLE OF CONTENTS

List of Tables

List of Figures

ABSTRACT

A study was conducted to determine the effects of several atropine dosage levels (0, 0.5, 1.0, 2.0, 3.0, 4.0 mg, administered intramuscularly) combined with ambient heat exposure (40 deg C, 40% RH) on the ability of soldiers to perform a task consisting of plotting sector-grid coordinate locations on military maps. Following acclimatization, eight soldier volunteers plotted grid coordinates on military sector maps for a ten-minute period daily as part of a larger study, under different series of daily drug administrations combined with heat exposure. No differences were observed in performance of the task between drug test days and control days, either in number of targets plotted or in mean errors. Furthermore, any drug effects on performance were so slight as to be offset by noticeable improvement in performance of the task due to practice. These results would seem to support the feasibility of atropine utilization as a chemical defense antidote for combat operations, since it had no observable effect on performance of an important and widely-employed operational military task.

1. INTRODUCTION

The importance of chemical weapons in future warfare and the likelihood of their deployment requires that effective antidotes be available as a defensive measure in the event of exposure of troops to chemical agents. Military doctrine for the use of antidotes involves the assumption that personnel will be able to inject themselves effectively with the correct dosages. However, there is a great potential risk that some individuals, through panic when faced with the threat of exposure, may prematurely inject themselves or overdose themselves as an attempted precaution, or both. Premature injection can be a serious matter, since the specific effects of the antidote itself in the absense of the agent to be counteracted may be considerably more severe than in combination with it, as intended in standard operating procedure. In this connection, since atropine is the current Army standard antidote for chemical agent exposure, it is important to determine its effects alone upon significant military performance tasks at dosage levels which could realistically be expected to occur in a battlefield situation.

Atropine is a well-known pharmacologic agent with a long history in medical therapy. Most of the research on human reactions to this drug have focused on biochemical and physiological effects. Two frequently observed physiological reactions which may be of military concern are increased heart rate and reduced sweating, because of their role in body heat dissipation during heavy physical work. These relationships have been investigated by Kolka, et al (1984), and by Levine, et al (1983). Changes in visual-ocular reactions may also be of military interest, and have been observed following 2 mg atropine administration. These changes have primarily taken the form of mydriasis, cycloplegia and loss of contrast sensitivity (Baker, et al, 1983).

Comparatively little research has been done on the effects of atropine on behavioral reactions, subjective symptomatology, and the ability to perform military tasks. Headley (1982) has reviewed and summarized the available literature on these topics, along with studies of biochemical and physiological reactions to atropine. The dosage levels used in the studies included in his review generally were 1-2 mg injected intramuscularly, although dosages as high as 12.25 mg were occasionally employed (Holland, et al, 1973; Marzulli and Cope, 1950; Miles, 1955; Stamper, et al, 1983; Wetherall, 1980). The behavioral tasks involved in these studies included reaction time, judgment capability, and perceptual and cognitive performance. The overall findings of this body of research were mixed, in that approximately half of the studies showed changes in performance following 2 mg atropine, while performance in the other studies was unaffected. Moreover, the tasks which were affected showed no consistent common basis to distinguish them from the tasks which were unaffected. Later studies involving higher dosages ranging between 6 and 12 mg have shown comparatively greater impairments in this type of performance, but no consistent trend has emerged as to the specific types of performance affected by atropine (Gordon and Frye, 1955; Moylan-Jones, 1969). It cannot be overlooked, also, that many of the effects which have been reported could very easily have been due to experimental confounding of the effects of atropine combined with the

influence of other situational stress factors. Finally, it should be noted that hallucinatory experiences have frequently been reported as a result of atropine administration.

In view of the mixed findings arising from the published literature on the effects of atropine on human performance weighed against the mandated use of atropine in a chemical emergency, it is essential to achieve a valid and clear assessment of the actual effects of atropine on the performance of realistic military tasks. Furthermore, since the standard Military Oriented Protective Posture (MOPP) ensemble generates a significant heat load on the user, it is equally important to determine the effects of the drug-heat interaction which could conceivably occur in the case of the MOPP-clad soldier having also self-administered atropine. Moreover, this problem may be amplified further in a tactical operation fought in a hot or hot-humid climatic area, where the heat load on the MOPP-clad soldier will be increased due to the ambient environment.

Because of the above considerations, the present study was conducted as part of a USARIEM project to evaluate the effects of graded dosage levels of atropine combined with ambient heat exposure on the capability of personnel to perform military tasks. The specific aspect of the project reported here concerns the effects of atropine on performance of a task based on plotting of grid coordinates on military tactical maps.

2. METHOD

Subjects

Eight healthy male soldier volunteers ages 21-26 years were employed. They received a preliminary medical screening to ascertain their physical fitness for participation.

Procedure

The subjects first completed an initial regimen of heat acclimatization consisting of treadmill walking in an ambient environment of 40 deg.C; 30% R.H. for two hours daily on four consecutive days. Following acclimatization, they underwent a schedule of daily tests and measurements over a total period of 15 days. Within this period, subjects were tested on alternate days, during which each received a different staggered order of drug dosages on a double-blind basis. All drug orders were made up of the same values: 0, 0.5, 1.0, 2.0, 3.0, 4.0 mg. All drug dosages were administered by intramuscular injection. A schedule of daily drug dosage levels is shown in Table I.

TABLE I

SCHEDULE OF ATROPINE DOSAGES (MG)
FOR INDIVIDUAL SUBJECTS

SUBJECT	TEST DAY*														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	0	.5	-	1	-	0	-	2	-	2	-	0	-	.5	-
2	0	.5	-	1	-	0	-	-	-	2	-	0	-	4	-
3	0	.5	-	1	-	0	-	2	-	2	-	0	-	3	-
4	0	.5	-	1	-	0	-	2	-	2	-	0	-	.5	-
5	0	0	-	0	-	0	-	0	-	.5	-	0	-	.5	-
6	0	.5	-	1	-	0	-	2	-	2	-	0	-	4	-
7	0	.5	-	1	-	0	-	2	-	2	-	0	-	2	-
8	0	.5	-	1	-	0	-	2	-	2	-	0	-	2	-

*Blanks indicate non-test days

Note that the subjects received placebo injections of normal saline solution on days 5, 10 and 16 (indicated as 0 in Table I); also, that on day 18, the last drug test day, different subjects received a variety of drug dosages (0.5, 2.0, 3.0 and 4.0 mg). All testing was performed in an environmental chamber set at an ambient temperature of 40 deg.C and 20% R.H. Core temperatures of all subjects were monitored continuously via rectal catheters. Performance measurements on each test day were preceded by two 50-min. periods of treadmill walking.

The map-plotting task consisted of identifying and plotting the locations of sector grid-coordinate pairs on a regulation Army military map depicting a terrain area with which none of the subjects had any previous experience. Each subject was furnished an individual copy of the terrain map mounted on a plotting board of the same size as the map area, a regulation artillery protractor, map pins and a pencil. Every subject also received a different printed list of grid-coordinates, which were to be located one pair at a time using the protractor, then marked with a map pin and circled neatly in pencil. The map pin was then withdrawn, and the subject then marked the next pair. All subjects worked independently. A preliminary training session was conducted prior to the main study, in which the subjects were instructed in the proper task performance, and then were given an intensive practice period under continuous supervision and correction. The training

session was continued until all subjects had mastered the task. On each day of the ensuing main experiment, each subject received a different list of grid-coordinates to be plotted, and completed as many as possible during a ten-minute work period. Testing was performed once each test day, approximately two hours after drug or placebo administration.

3. RESULTS AND DISCUSSION

The individual grid-coordinate points plotted by each subject on the maps issued on each experimental day were first located and verified. These points were then converted to their corresponding numerical grid-coordinate values using an automated graphics tablet, outputting to a VAX-11 computer. This was done by intersecting the cross-hairs of the tablet over each plotted point, and storing the resulting values in individual data files for each subject. A computer program then calculated the numerical differences between the plotted values and their corresponding true values (the original grid-coordinates issued to the subjects to be plotted), and printed out these differences as error scores in units of meters. These values comprise the data upon which the analysis of results was based. A summary of these values is presented in Table II, along with the associated group means of the individual plot totals and of the individual error means.

TABLE II
SUMMARY OF TOTAL TARGETS PLOTTED, ARITHMETIC MEANS
AND STANDARD DEVIATIONS OF PLOTTING ERROR
AS A FUNCTION OF ATROPINE DOSAGE LEVELS

	DAY 1		DAY 2		DAY 3		DAY 4		
S	NO.	MEAN S.D.	NO.	MEAN S.D.	NO.	MEAN	NO.	MEAN S.D.	S.D.
1	15	10.04 12.21	22	7.97 105.84	23	33.92 5.34	18	41.88	2 .33
2	12	4.30 2.47	24	5.11 2.66	28	44.45 171.56	30	3.35 2.53	
3	16	2.82 1.49	22	7.62 20.20	26	4.23 1.63	30	4.52 1.79	
4	13	28.01 63.12	27	3.34 2.49	22	37.18 149.63	22	12.06 24.49	
5	11	34.27 19.52	25	43.06 25.69	26	39.38 24.55	30	38.44 30.69	
6			26	5.17 4.98	27	3.99 2.32	27	3.85 2.53	
7			30	4.13 1.89	29	4.21 4.66	30	2.66 1.85	
8			21	22.69 86.91			24	99.98 280.71	
M	13	15.89 17.79	25	12.39 19.63	26	23.91 65.70	26	25.84 43.74	

TABLE II (CONT'D.)

	DAY 5		DAY 6		DAY 7		DAY 8	
S	NO.	MEAN	NO.	MEAN	NO.	MEAN	NO.	MEAN
1	21	40.55 174.34	19	9.47 20.45	14	5.86 3.03	19	4.71 2.67
2	30	7.22 17.33	30	5.75 6.39	30	3.72 2.06	30	9.66 19.61

3	26	2.99			30	6.22	29	11.58
		1.82				18.44		23.66
4	27	6.50	30	2.92	30	12.59	29	10.52
		18.66		1.84		39.98		24.03
5	30	34.01	27	39.13	29	59.65	29	41.39
		26.23		25.33		81.30		35.66
6	27	3.93	29	50.00	26	11.84	30	5.24
		3.78		246.61		27.30		2.86
7	30	43.97	30	3.86	30	2.98	30	7.14
		222.04		2.21		1.4		13.99
8	21	3.58	15	4.58	14	14.09	23	8.98
		2.02		2.85		36.91		20.79
M	26	17.84	26	16.53	25	14.62	28	12.40
		58.28		43.67		26.3		18.45

In order to assess possible overall changes in map-plotting performance due to atropine dosage levels, two subjects x treatments analyses of variance were conducted, one on the data for individual numbers of targets plotted daily, and another on the individual arithmetic means of daily errors in plotting (true position - plotted position). The results of these analyses yielded a significant main effect only for the number of targets plotted daily ($F=6.67$; $df=7,6$; $P=<.02$), and for differences among subjects ($F=16.94$; $df=6,7$; $P=<.001$). No significant effects were obtained for the the mean plotting error data.

In order to determine the possible presence of systematic trends across the daily performance (drug) conditions, the group means of the total number of targets plotted and of the plotting error values in meter units were plotted graphically, and are shown as Figures 1 and 2.

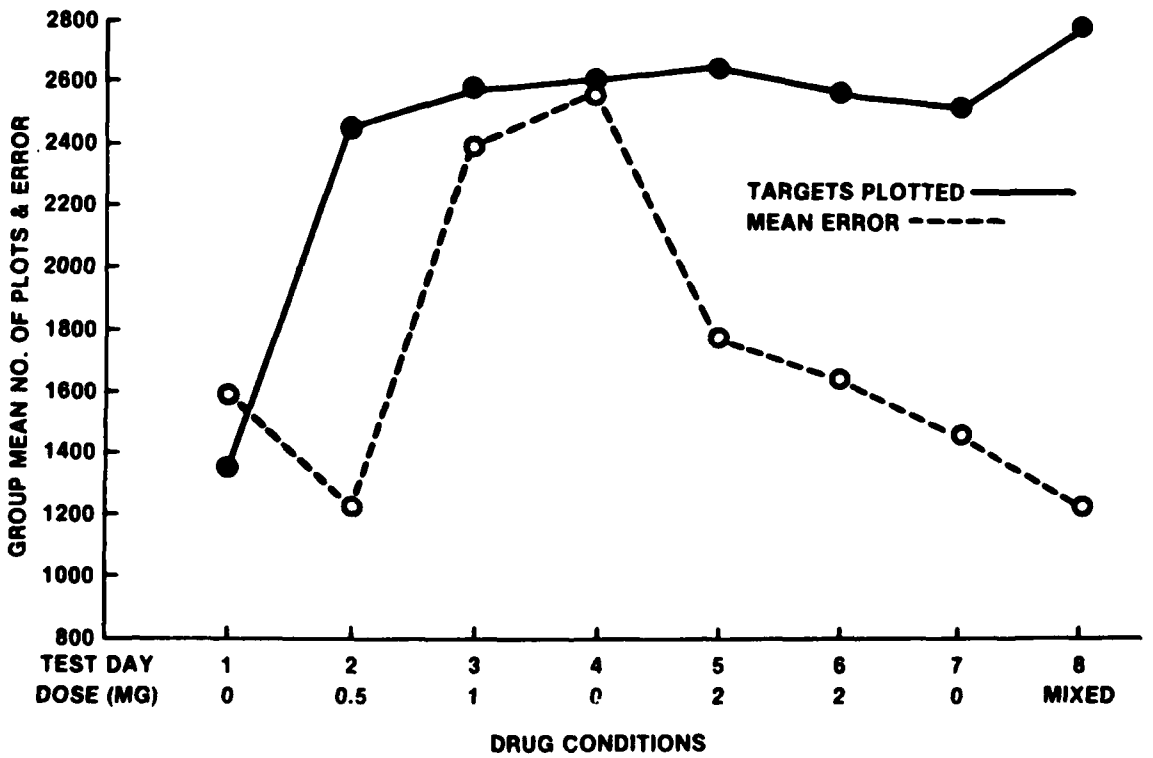

Figure 1. Group mean errors and number of targets plotted as a function of daily sequence of atropine dosage

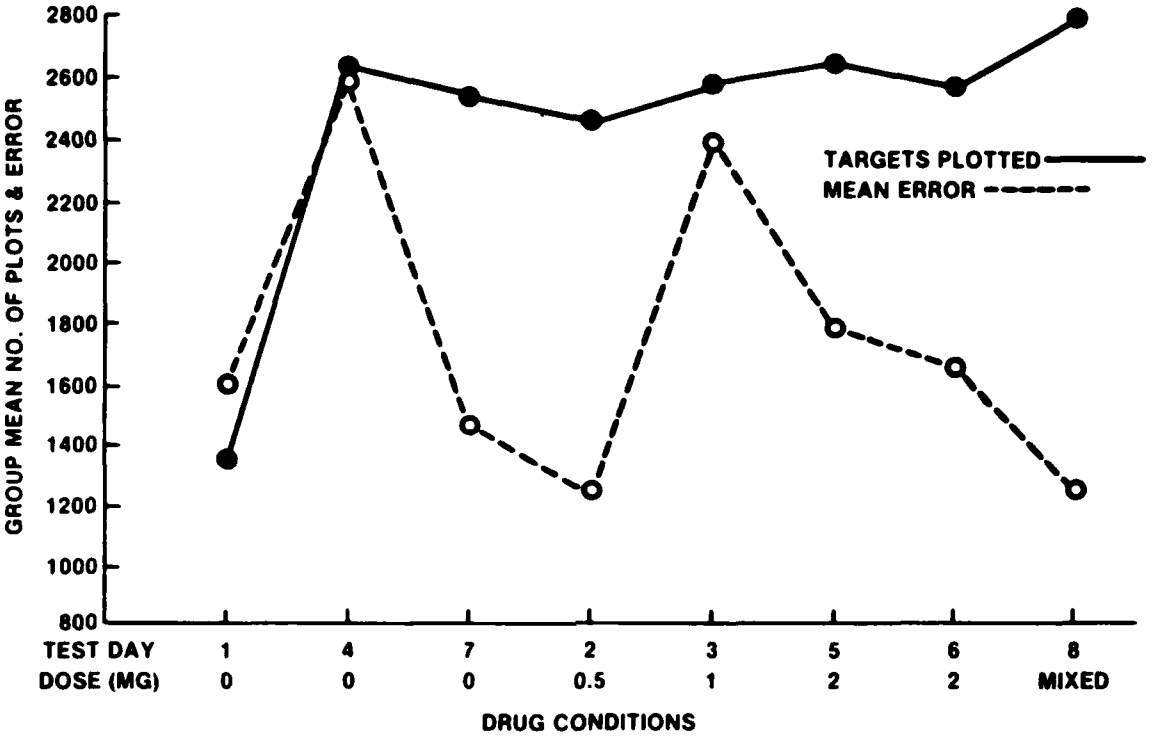

Figure 2. Group mean errors and number of targets plotted as a function of increasing atropine dosage

In Figure 1, the independent variable of atropine dosage is arrayed on the abscissa according to the daily sequence of occurrence. The same values are presented again in Figure 2, but with the abscissa values arrayed in increasing order of dosage magnitude, and in daily sequence of occurrence where the same dosage was repeated. It can be seen in Figure 1 that the total number of targets plotted increased abruptly on the second day of the study, and remained at virtually the same level thereafter regardless of increases in atropine dosage. A rather different result is evident for mean plotting error, in that increases in error occurred during the first four days, and then diminished markedly on the remaining four days. However, the error increases occurred at relatively low dosage levels, whereas the decreases in

error occurred at the highest dosage levels of the study. In addition to this, note that the single highest error level occurred on a zero-dose test day (Day 4). In contrast, the two days of highest dosage (2 mg on Days 5 and 6) produced relatively low error values compared to previous days at lower dosage levels. These overall findings imply a definite practice effect in performance of the map plotting task, which undoubtedly is the factor reflected in the significant main effect for the analysis of number of targets plotted. Although these results are not meaningful in terms of drug effect, they do indicate that the effects of atropine were slight enough to be offset by changes in performance due to practice. The overall trend in performance of this task during the course of the study can probably be attributed to inadequate practice in map plotting prior to conduct of the main experiment, a condition which was unavoidable due to administrative circumstances.

In Figure 2, where the same data are presented according to increasing dosage level, there is no indication that the amount of administered atropine had any systematic influence on the performance of map plotting. The number of targets plotted follow a consistent level of output after an initial increase in production from the first to the second day. With regard to plotting error, there appears to be no practical difference between error levels at low or no dosages and those at 1 and 2 mg. Therefore, one must conclude that the overall effect of atropine on map plotting performance was negligible, or at most, a slight enough effect to be easily overcome by the effects of practice and experience with the task.

4. CONCLUSIONS

The results of this study give no indication that doses of atropine up to 2 mg injected intramuscularly have any significant influence on the important and commonly performed task of grid-coordinate plotting on military maps. These findings may have more significance than would appear directly, when it is considered that the map plotting task employed in this study has been shown in previous work to be highly affected both by hypoxia and by heat stress. The fact that atropine had little effect on this task lends support to consideration of its use as a field antidote in military operations involving chemical defense.

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